REMARKS

Reconsideration of this application is respectfully requested. Claims 11-19, 26, 30, 38, and 39 have been canceled without prejudice. Claim 1 has been amended to recite a tablet comprising tacrolimus dispersed in a vehicle, where the vehicle includes polyethylene glycol (PEG) having an average molecular weight of at least 1500 and a poloxamer. Claims 2-10, 20-25, 27-29, 31-37, 40-44 have been amended for clarity and to replace the terms "solid composition" (or "composition" or "dosage form") and "active ingredient" with the terms "tablet" and "tacrolimus", respectively. The exemplary language in claims 20, 25, 32, and 36 has been deleted. Claims 20-22 and 31 have been amended to depend from claim 1 rather than claims 10 and 19. Claims 35 has been amended to recite that the tablet includes compressed particles. Claim 37, which has only been rejected for obviousness-type double patenting, has been rewritten in independent form and to recite that the tablet includes compressed particles of (i) tacrolimus dispersed in a vehicle of PEG and a poloxamer and (ii) one or more pharmaceutically acceptable excipients. Claims 40 and 41 have been amended to depend from claims 1 and 33, respectively, instead of claim 38. Claim 44 has been amended to recite that the silicon dioxide comprises colloidal silica. Claim 51 has been amended to recite a method of preparing a tablet of claim 1 by dispersing tacrolimus in a vehicle of PEG and poloxamer, and forming a tablet from the dispersion. Claim 52 has been added. Support for these claim amendments is found at, for example, paragraphs 117 and 194 and Examples 1, 3, 9, 10, 14, and 16 of the published version of this application (US 2006/0287352) and original claims 19-22. Claims 1-10, 20-25, 27-29, 31-37, 40-44, 51, and 52 are pending and at issue.

Indefiniteness Rejection

Claims 15, 16, 20, 25, 26, 30, 32, 36 and 44 have been rejected as indefinite, for either the use of a trademark, or a broad limitation together with a narrower limitation.

Claims 15, 16, 26, and 30 have been canceled without prejudice. The narrower ranges recited in claims 20 and 36 have been deleted. The trademarks in claims 25, 32, and 44 have been deleted. Accordingly, Applicants respectfully request withdrawal of this rejection.

Anticipation Rejections

Claims 1-8, 10-13, 15-19, 23, 24, 27-42 and 51 have been rejected as anticipated by EP 1064942 (Yamashita).

Claims 11-13, 15-19, 30, 38, and 39 have been canceled without prejudice.

Yamashita does not disclose or suggest a tablet comprising tacrolimus in a vehicle comprised of PEG having an average molecular weight of at least 1500 and poloxamer, as called for in the pending claims. Accordingly, Yamashita does not anticipate the pending claims, and Applicants respectfully request withdrawal of this rejection.

Claims 1-19, 22-36 and 38-44 have been rejected as anticipated by WO 01/37808 (Patel).

Claims 11-19, 26, 30, 38, and 39 have been canceled without prejudice.

Patel does not disclose or suggest a tablet comprising tacrolimus in a vehicle comprised of PEG having an average molecular weight of at least 1500 and poloxamer, as called for in the pending claims. *See* p. 8, the first two lines, of the Office Action. Accordingly, Patel does not anticipate the pending claims, and Applicants respectfully request withdrawal of this rejection.

Obviousness Rejection

Claims 1-36 and 38-44 have been rejected as obvious over Patel in view of WO 01/95939 (Koretke). According to the Examiner, Patel discloses a "solid controlled release tacrolimus formulation comprising various hydrophilic and hydrophobic components" (p. 7, last paragraph, of the Office Action). The Examiner concludes that it would have been obvious to use the poloxamer/PEG carrier of Koretke in the tacrolimus formulation in Patel.

As a first matter, Patel does not teach a tacrolimus formulation comprising "various hydrophilic and hydrophobic components." Example 20 in Patel discloses a tacrolimus composition containing Solulan C-24 (i.e., PEG24 cholesterol ether)[1], distilled monoglycerides, and deoxycholic acid. Although Patel lists pages of components that can potentially be used in a dosage form, there is no teaching that would have led one of ordinary skill in the art to a tablet comprising tacrolimus dispersed in a mixture of PEG and poloxamer.

Koretke does not cure Patel's deficiencies. Koretke is directed to solid dispersions comprising a PEG and poloxamer mixture. Koretke prepares the solid dispersion by co-melting of a drug, poloxamer surfactant, and polyethylene glycol, followed by filling of the molten material into capsule shells or molds and allowing the material to cool (p. 6, lines 32-38). The co-melt material contains at least 60% PEG, rendering it unsuitable for tabletting. PEG is waxy and has a low melting point. During tabletting, the PEG would be expected to melt under typical compression and frictional forces of the tabletting machine (from about 1000-3000 kg), stick to the die and punches, and not be ejectable from the machine. *See* the attached Declaration of Dr. Reza Fassihi, ¶10-11 (Dr. Fassihi is a professor of Biopharmaceutics and Industrial Pharmacy at Temple University.). Koretke specifically distinguishes its hot fill method from prior known methods of forming solid dispersions, such as tablets:

[1] *See* p. 79, below the table in Example 3, of Patel.

> "This property distinguishes this invention from known solid dispersion dosage forms in which [the] solid dispersion of drug and PEG were milled and filled into capsules or tableted."

(Koretke, p. 6, lines 35-38).

Accordingly, a skilled artisan would not have used Koretke's method and formulation to make a tacrolimus tablet as presently claimed.

For the foregoing reasons, Patel alone or in combination with Koretke fails to render obvious the presently claimed tablet. Applicants, therefore, respectfully request withdrawal of this rejection.

Double Patenting Rejection

Claims 1-44 and 51 are provisionally rejected for obviousness type double patenting over each of (i) claims 59, 66, 72-74, 83-85 and 90 of co-pending Application No. 10/574,125, (ii) claims 1, 3-11, 13-29, 31-34, 36, 37, 40-44 and 53-56 of co-pending Application No. 10/569,863, (iii) claims 1, 8, 10, 17-23, 26-32, 34, 36, 37, 63 and 64 of co-pending Application No. 10/513,807, and (iv) claims 1-50 of co-pending Application No. 11/885,992.

Submitted herewith is a terminal disclaimer over U.S. Serial No. 10/513,807. Accordingly, Applicants respectfully request withdrawal of the provisional rejection over this application.

No subject matter has been allowed in the three remaining applications (10/574,125, 10/569,863, and 11/885,992). Accordingly, Applicants respectfully request that the provisional rejections with respect to these three applications be held in abeyance until the finding of allowable subject matter in one or more of them.

In view of the above amendment and remarks, Applicants believe the pending application is in condition for allowance.

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Respectfully submitted,

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